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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 19

Application Number: 09/863,824
Filing Date: May 23, 2001
Appellant(s): TURNER ET AL.

Lance Ishimoto
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 7/14/2003.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

Appellant's brief includes a statement that there are no related appeals or interferences

(3) Status of Claims

The statement of the status of the claims contained in the brief is incorrect. Appellants have indicated that in the Advisory Action mailed on 6/3/2003, the 35 USC 112, second paragraph rejection applied to claim 2 was maintained. However, it is noted that on page 2 of the Advisory Action (mailed 6/3/2003), paragraph 2, the Examiner clearly indicated that the amendment to claim 2 filed on 5/9/2003 was deemed sufficient to overcome the 35 USC 112, second paragraph rejection previously applied. In addition, item 7 of the Advisory Action form PTO-303 mailed 6/3/2003 was clearly marked to indicate that the proposed amendments were entered.

(4) Status of Amendments After Final

The Appellant's statement of the status of amendments after final rejection contained in the brief is incorrect. Appellants assert that amendments to claim 2 and the abstract were not entered by the Examiner following the response to the Final Action mailed on 5/5/2003. As indicated above, the Advisory Action on page 2, paragraph 2, clearly states that the amendment to claim 2 filed on 5/9/2003 was deemed sufficient to overcome the 35 USC 112, second paragraph rejection previously applied and item 7 of the Advisory Action form PTO-303 was clearly marked to indicate that the proposed amendments were entered. It is also noted that there is no record in Appellant's response filed on 5/9/2003 of an amendment to the Abstract nor there is any marked-up copy of the Abstract which would indicate Appellant's submission of an amended Abstract.

(5) Summary of Invention

The summary of invention contained in the brief is substantially correct. However, it includes several statements in regard to the alleged uses of the present invention which are appropriately found in the argument's section of the Brief and will be addressed in the Response to Arguments section of this Answer.

(6) Issues

The Appellant's statement of the issues in the brief is correct. For the record, it is noted that while Appellants have indicated in sections III and IV of the appeal brief that amendments to claim 2, filed on 5/9/2003 in response to the Final Action mailed on 12/2/2002, were not entered, Appellants have not stated in section VI of the appeal brief that there is an indefiniteness issue in regard to claim 2, as would have been the case if the 35 USC 112 second paragraph rejection would have been maintained as asserted by Appellants in sections III and IV of the appeal brief.

(7) Grouping of Claims

The brief contains a statement indicating that claims in each of the issues shall stand or fall together as a group

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

Bork, Genome Research, 10:398-400, 2000

Broun et al., Science 282:1315-1317, 1998

Colige et al., PIR accession number T18517, October 15, 1999

Lawler et al., PIR accession number TSHUP1, August 23, 1987

Multimegabase sequencing group, SPTREMBL accession number O95432, May 1, 1999

Seffernick et al. , J. Bacteriol. 183(8):2405-2410, 2001

Smith et al., GenBank accession number AL050320, October 25, 2002

Van de Loo et al., Proc. Natl. Acad. Sci. 92:6743-6747, 1995

Whitehead et al., GenBank accession number AL133463, October 24, 2002

Witkowski et al., Biochemistry 38:11643-11650, 1999

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 101

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 2-3 and 6-7 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Claims 2-3 and 6-7 are directed to a polynucleotide encoding the polypeptide of SEQ ID NO: 2, expression vectors comprising said polynucleotides, and host cells comprising said expression vectors.

The specification discloses that the polynucleotides of the instant application encode proteins which share structural similarities with mammalian thrombospondins (page 1, line 30- page 2, line 2). The specification further states that the polypeptides encoded by the polynucleotides of the instant invention share structural similarity to several proteins including, but not limited to, mammalian thrombospondins, semaphorins, metalloproteinases, and serine palmitoyltransferases. (page 16, lines 5-13).

While the specification does not specifically state a biological function for the polypeptide of SEQ ID NO: 2 and the corresponding polynucleotide (SEQ ID NO: 1), it appears to assert that the polynucleotide of SEQ ID NO: 1 may encode a new thrombospondin. However, the claimed invention does not meet the utility requirements for the following reasons.

There is no experimental evidence to support the assertion that the claimed polynucleotides encode a polypeptide having thrombospondin activity. The alleged function for the claimed polynucleotides has been determined solely on the basis of structural similarity (i.e. sequence homology). The state of the art clearly teaches the unpredictability of assigning function based on sequence homology

and acknowledges that small changes can drastically change function. Bork (Genome Research, 10:398-400, 2000), Broun et al. (Science 282:1315-1317, 1998), Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995), Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) and Witkowski et al. (Biochemistry 38:11643-11650, 1999) are examples of the state of the art in regard to the unpredictability of accurately assigning function based on structural homology.

Bork teaches the pitfalls associated with comparative sequence analysis for predicting protein function because of known error margins for high-throughput computational methods. Bork also indicates that one of the causes of this inaccuracy is that the quality of data available is still insufficient, especially data relating to protein function. Furthermore, Bork teaches that protein function is context dependent, and both molecular and cellular aspects must be considered (page 398). Van de Loo et al. teaches that polypeptides of approximately 67% homology to a desaturase from *Arabidopsis* were found to be hydroxylases once tested for activity. Broun et al. teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform a hydrolase to a desaturase. Witkowski et al. teaches that one amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Seffernick et al. teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different biological function.

Appellant's own specification discloses that the polypeptide encoded by the polynucleotide of the instant application share structural similarity with several proteins of different function (see discussion above). The closest structural homolog found is disclosed by Multimegabase sequencing group (SPTREMBL accession number O95432, May 1, 1999) as a serine palmitoyltransferase having 36.8% sequence identity to SEQ ID NO: 2. A human thrombospondin disclosed by Lawler et al. (PIR accession number TSHUP1, August 23, 1987) is 5% sequence identical to the polypeptide of SEQ ID NO: 2

whereas a procollagen I N-proteinase disclosed by Colige et al. (PIR accession number T18517, October 15, 1999) presents 4.9% sequence identity to the polypeptide of the instant application. See attached alignments. The specification is completely silent in regard to the critical structural elements in the polynucleotide of SEQ ID NO: 1 or the polypeptide of SEQ ID NO: 2 which are indicative of thrombospondin activity. In view of the unpredictability of annotating function based on sequence homology, as evidenced by the teachings of Bork, Brenner, Smith et al., Broun et al., Van de Loo et al., Seffernick et al. and Witkowski et al. as well as the low % sequence homology between the polynucleotides/polypeptide of the instant application and polynucleotides/polypeptides of the prior art having thrombospondin function, one of skill in the art cannot reasonably conclude that the asserted function for the polypeptide encoded by the claimed polynucleotides is that of a thrombospondin absent additional supporting evidence such as an indication of which are the critical structural elements present in the claimed polynucleotides characteristic of other polynucleotides encoding thrombospondins or even experimental evidence of the claimed function. In the instant case, the specification fails to provide any information or experimental evidence which would support Appellant's asserted biological function, other than the disclosure of the function of the closest structural homologs.

Even if one assumes that the asserted function of the polypeptide of SEQ ID NO: 2 is that of a thrombospondin, one cannot determine which type of thrombospondin is being encoded by the polynucleotide of the instant invention (SEQ ID NO: 1) or what is the function of the polypeptide of SEQ ID NO: 2. Thrombospondins, as known in the art, belong to a family of at least 5 members in vertebrates, each with diverse functions. In the absence of some knowledge or guidance as to the type of thrombospondin and/or the biological processes in which the polypeptide of SEQ ID NO: 2 is involved, one of skill in the art cannot determine the actual biological function of the protein of SEQ ID NO: 2. Therefore, the specification fails to disclose sufficient information to conclude that there is a substantial

and specific utility associated with the thrombospondin polynucleotide/polypeptide of the instant invention.

The specification discloses that thrombospondins are extracellular proteins that have been implicated in blood clotting, angiogenesis, diabetes, inflammation, wound healing, and cancer (page 1, lines 23-25). The specification also discloses that the polynucleotides of the instant invention can be used to screen collections of genetic material from patients who have a particular condition (page 7, lines 26-29). Other uses for the polypeptide or the corresponding polynucleotide include protein therapeutics, identification of related polypeptides/polynucleotides, and screening of pharmaceutical reagents useful in the treatment of diseases (page 19, lines 1-14). In addition, the specification discloses that the polynucleotides of the instant application can be used for mapping a unique gene to a particular chromosome (page 2, lines 25-28) and as hybridization probes or in gene chips (page 5, line 23-page 7, line 33)

While the specification asserts several uses for the claimed polynucleotides, these utilities are not considered substantial and specific for the following reasons. The specification fails to disclose sufficient information in regard to the biological significance and further characterization of the claimed polynucleotides and the protein encoded thereby, such as (1) the targets (i.e. interacting proteins) of the alleged thrombospondin, (2) the biological processes or pathways in which the targets or the polypeptide of SEQ ID NO: 2 are involved, (3) specific conditions/diseases associated with the expression, or lack thereof, of the polynucleotide of SEQ ID NO: 1, such that a specific use for the claimed polynucleotides would be apparent. If information in regard to the biological role of the claimed invention were to be presented, several utilities could be apparent for the claimed polynucleotides and the corresponding polypeptide, such as detection of the targets in samples, or isolation of modulators which can be used to regulate the processes in which the alleged thrombospondin is involved. However, these utilities require additional information which is not presented by the specification. As known in the art and admitted by

Appellants in the specification, thrombospondins are associated with many different biological processes. Furthermore, thrombospondins belong to a large and diverse family of proteins with diverse roles in many physiological and pathological processes, therefore one would expect a thrombospondin to be rather specific in regard to its targets. Since, the substrates, the cellular function of the thrombospondin and its targets, and the biological processes associated with the targets/ thrombospondin are all unknown, the utilities recited in the specification are not substantial since they will require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. See e.g., *Brenner v. Manson,* 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). The instant situation is analogous to the lack of substantial utility examples provided by MPEP § 2107.01 in that basic research is required to study the properties of the claimed polynucleotides and the corresponding polypeptide as well as the mechanisms in which the claimed polynucleotides are involved. In addition, while one could argue that some of the recited uses are specific, such as being a probe to be used in microarrays or in mapping of nucleotides in a particular chromosome, it is noted that these uses are not specific due to the fact that all other human polynucleotides can be used as probes in microarrays or in mapping of nucleotides in the chromosome. Since the instant specification does not disclose an specific and substantial "real world" use for the polynucleotide of SEQ ID NO: 1 or a polynucleotide encoding the polypeptide of SEQ ID NO: 2, then the claimed invention as disclosed does not meet the requirements of 35 U.S.C. §101 as being useful.

Claims Rejections – 35 USC §112, first paragraph – Enablement/Utility

Claims 2-3 and 6-7 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantial and specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

(11) Response to Argument

A. Do Claims 2-3 and 6-7 lack patentable utility?

On page 4 of the Brief, Appellants state that they strongly disagree with the rejection of claims 2-3 and 6-7 under 35 USC § 101 as lacking a patentable utility since according to Appellants, the specification details a number of specific and substantial utilities for the claimed polynucleotides. Appellants indicate that as evidenced by U.S. Patent No. 5155038, 5981222 and 6013781, thrombospondins and semaphorins protein homologs have been subject to considerable scientific scrutiny. Appellants further argue that additional utilities for the claimed invention include use as reagents in assays for screening for compounds that can be used as pharmaceutical reagents to treat mental, biological, or medical disorders, determining temporal and tissue specific gene expression patterns using gene chips, mapping specific regions of a human chromosome, identifying protein coding regions, determining the genomic structure, determining intron/exon splice junctions and use of described polymorphisms in diagnostic assays such as forensic analysis, human population biology and paternity determinations.

The Examiner acknowledges the teachings of U.S. Patent No. 5155038, 5981222 and 6013781, and agrees that thrombospondins and semaphorins have been the subject of scientific study. However, it is noted that in the instant case, the closest structural homolog found for the polypeptide of SEQ ID NO: 2 is not a thrombospondin but rather a serine palmitoyltransferase (Multimegabase sequencing group, SPTREMBL accession number O95432, May 1, 1999), and the closest functional homolog (Lawler et al., PIR accession number TSHUP1, August 23, 1987) is only 5% sequence identical to the polypeptide of SEQ ID NO:2. Furthermore, another structural homolog having almost 5% sequence identity to the polypeptide of SEQ ID NO: 2, has procollagen I N-proteinase activity. As such, one of skill in the art would require further research to actually determine if the biological function of the polypeptide of SEQ ID NO: 2 is indeed that of a thrombospondin. Furthermore, the specification fails to present any

experimental evidence to support the assertion that the claimed polynucleotides encode a polypeptide having thrombospondin activity. Even if the polypeptide of SEQ ID NO: 2 is a thrombospondin, it is unclear as to how one of skill in the art can reasonably conclude that the claimed polynucleotides have a specific and substantial utility, if the specification is completely silent in regard to the type of thrombospondin disclosed, its biological target, the biological processes where it is involved or which diseases/disorders are associated with its expression, or lack thereof. As admitted by Appellants, thrombospondins are extracellular proteins that have been implicated in a diverse array of biological processes, i.e. blood clotting, angiogenesis, diabetes, inflammation, wound healing, and cancer (page 1, lines 23-25). As known in the art, thrombospondins belong to a family of at least 5 members in vertebrates, each with diverse function. In addition, the specification is completely silent as to how one can use the claimed polynucleotides or polymorphisms in forensics, human population biology, or paternity determination. Therefore, in the absence of any information further characterizing the biological function of the polypeptide of SEQ ID NO: 2, such as thrombospondin type, targets, biological processes, or diseases/disorders associated with the expression of the claimed polynucleotides, or lack thereof, the utilities recited above for the claimed polynucleotides, i.e. as reagents in assays for screening for compounds that can be used as pharmaceutical reagents to treat mental, biological, or medical disorders, determining temporal and tissue specific gene expression patterns using gene chips, forensics analysis, human population biology and paternity determinations, are not substantial since they will require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. See e.g., *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). In regard to uses such as mapping specific regions of a human chromosome, identification of protein coding regions, determination of the genomic structure, determination of intron/exon splice junctions, it is noted that these uses are not specific due to the fact that other human polynucleotides can be used for chromosome mapping, identification of protein coding regions, determination of intron/exon splice junctions, and

determination of genomic structure. Therefore, the specification fails to disclose sufficient information to conclude that there is a substantial and specific utility associated with the thrombospondin polynucleotide/polypeptide of the instant invention.

On page 5 of the Brief, first paragraph, and continuing on page 6, Appellants indicate the present invention has a number of substantial and credible utilities, not the least of which relates to polymorphisms identified in the polynucleotides of the instant application at positions 364, 365, and 535 of the polynucleotide of SEQ ID NO: 1. Appellants submit that these polymorphisms have a significant and specific utility in the fields of forensic science, human population biology, and in the resolution of paternity issues. Appellants also submit that these utilities are not only credible but well established and known to one of skill in the art. Therefore, Appellants conclude that these are "real world" utilities which must be useful. It is Appellant's opinion that the presence of additional polymorphic markers does not mean that the present polynucleotides lack utility. According to Appellants, the polymorphisms described in the instant application can be used in forensic analysis exactly as it was described in the specification since individual members of a population can be distinguished based on the presence or absence of the described polymorphisms. As such, it is Appellant's opinion that there is no need for additional research. Furthermore, Appellants submit that simply because the use of this polymorphic marker will necessarily provide additional information on the percentage of a particular population that contains this marker, does not mean that additional research is needed for the polymorphic marker to be of use in forensic science.

The Examiner acknowledges the disclosure of two polymorphisms in the specification. However, the Examiner disagrees with Appellant's contention that the claimed polynucleotides have utility in forensic analysis or in paternity determination. As known in the art, polymorphisms are found in almost any human gene. As such, any polymorphism can, in principle, be used in forensic analysis or in paternity determination. In the instant case, neither the specification nor the art teaches any correlation between the presence or absence of the polymorphisms disclosed and a specific identifying characteristic,

such that one can distinguish one individual or population from another. Information which would allow one to conclude that the asserted uses in forensics or paternity determination are specific and substantial, such as ethnic background of those populations carrying them, frequencies in the populations carrying them, X/Y chromosomal linkage, or specific disorders/conditions associated with their presence or absence, is completely lacking. In addition, as indicated in the Advisory Action and reiterated herein, there is no teaching as to the biological significance of these polymorphisms either. Therefore, in the absence of a correlation between these polymorphisms and some identifying characteristic, one cannot reasonably conclude that the claimed polynucleotides have a real world use in forensic analysis or paternity determination. Furthermore, determining the correlation between these polymorphisms and a specific identifying characteristic would require additional research since the specification provides no clue as to the possible characteristics associated with the presence or absence of such polymorphisms. Thus, contrary to Appellant's assertion, the claimed polynucleotides lack patentable utility as tools in forensic science or in paternity determination.

On page 6 of the Brief, first paragraph, and continuing on page 7, Appellants submit that this is not a case of potential utility. According to Appellants, the polymorphic markers of the instant application will distinguish one population from another and that in the worst case scenario, this marker is useful to distinguish 50% of the population. As such, the ability to eliminate 50% of the population in forensic analysis is clearly a real world, practical utility. Appellants further submit that the Final Action seems to be confusing the requirements of a specific utility with a unique utility. According to Appellants, the fact that other polymorphic markers have been identified in other genetic loci does not mean that Appellant's identification of a polymorphic marker in the polynucleotide of SEQ ID NO: 1 is not specific, and cite *Carl Zeiss Stiftung v. Renishaw* PLC, 20 USPQ2d 1101 (Federal Circuit 1991) in support of their arguments. Appellants argue that the proper standard for utility under 35 USC § 101 is specific and not unique and that if every invention were required to have unique utility, the PTO would no

longer be issuing patents on batteries, automobile tires, golf balls, golf club and treatments for a variety of human diseases because examples of each of these have already been described and patented. Furthermore, it is Appellant's opinion that if a composition needed to be unique to be patented, the entire class/subclass system would be an effort in futility.

While in principle a polymorphism can be used to distinguish one population from another, it is noted that neither the specification nor the art teaches which segment of the population can be distinguished by the disclosed polymorphisms or which are the characteristics common to those individuals carrying such polymorphisms. There is no disclosure of the biological role of these polymorphisms either. While Appellants argue that the claimed polynucleotides can be used as markers to distinguish at least 50% of the population, the specification fails to disclose any evidence showing that the instant polymorphisms are found in at least 50% of the population. In fact, it provides no clue as to which percentage of the population carries the polymorphisms, or whether these polymorphisms are associated with individuals having a specific ethnic background, and their frequencies in those individuals.

The Examiner acknowledges the findings in *Carl Zeiss Stiftung v. Renishaw* PLC and agrees that the legal standard under 35 USC § 101 is specific and not unique. However, the Examiner disagrees with Appellant's contention that the Examiner has confused specific utility with unique utility. The Examiner is not contending that the claimed polynucleotides lack utility because other polymorphic markers have been described previously but rather due to the complete lack of information as to what is specifically being detected with these polymorphic markers, i.e. which populations are being distinguished by the presence or absence of these markers or which are the specific characteristics an individual carrying these markers should have. In the absence of this information, the asserted use of the claimed polynucleotides as polymorphic markers is not specific and substantial since other polynucleotides also can be used as polymorphic markers. It is noted that what makes a polymorphic marker specific is its ability to distinguish a certain population from another or to identify an individual having a specific characteristic.

This is analogous to a baseball bat, a hockey stick or a golf club being used as sticks but each having a specific use to play baseball, hockey or golf. Thus, the Examiner has not used the requirements for unique utility, as asserted by Appellants, in view of the fact that there is not even a description of the populations which can be distinguished by these polymorphic markers nor there is any information as to which identifying characteristics are associated with the presence or absence of these polymorphisms in an individual, or the frequency of these polymorphisms in any population. The asserted utility as polymorphic markers is not a substantial utility in view of the fact that additional research is needed to identify which populations are associated with these polymorphic markers, and/or which characteristics are associated with the presence or absence of these polymorphisms, such as diseases, disorders, or ethnic background.

On page 7 of the Brief, first paragraph, Appellants submit that the asserted forensic utility is specific because it cannot be applied to just any nucleic acid. According to Appellants, the basis for forensic analysis is the fact that a polymorphic marker is not present in all other nucleic acids but it is specific and unique to only a certain subset of the population. As such, the presently claimed invention must meet the requirements for utility under 35 USC § 101.

Appellant's argument that the asserted forensic utility is specific because it cannot be applied to just any nucleic acid is not found persuasive in view of the fact that the specification has not disclosed any association between the presence or absence of these polymorphisms with a specific subset of the population, as asserted, nor has it provide any clue as to any identifying characteristic associated with such polymorphisms, such as ethnic background, X or Y chromosomal linkage, frequency within a population, or disorders/diseases associated with their presence or absence. As such, one cannot reasonably conclude that the claimed invention meet the requirements for utility under 35 USC § 101.

On page 7 of the Brief, second paragraph, Appellants indicate that a claim need not describe the invention, such description being the role of the disclosure and that it is well established that an inventor

is not required to understand the theory of how his invention works. Appellants cite *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.* and *Micro Motion Inc. v. Exac Corp.* in support of their arguments. Appellants submit that there is a contradiction between the Final Action on page 3 which states that the specification does not disclose a function for the disclosed protein and the Advisory Action on page 4, lines 10-15 since the Advisory Action makes reference to Appellant's assertion of thrombospondin function for the polypeptide encoded by the claimed polynucleotides and how even if the polypeptide of SEQ ID NO: 2 is a thrombospondin, the claimed polynucleotides would lack specific utility since thrombospondins belong to a family of at least 5 members in vertebrates.

The Examiner acknowledges (1) the findings in *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.* and *Micro Motion Inc. v. Exac Corp.*, (2) that a claim need not describe the invention, and (3) that an inventor is not required to understand the theory of how his invention works. However, in the instant case, the specification fails to disclose essential information which would satisfy the 35 USC § 101 requirements for patentably utility. As discussed above and reiterated herein, in view of the fact that the closest structural homolog found for the polypeptide of SEQ ID NO: 2 is not a thrombospondin but rather a serine palmitoyltransferase (Multimegabase sequencing group, SPTREMBL accession number O95432, May 1, 1999), and the closest functional homolog (Lawler et al., PIR accession number TSHUP1, August 23, 1987) is only 5% sequence identical to the polypeptide of SEQ ID NO:2, and in the absence of any experimental evidence corroborating thrombospondin activity for the polypeptide of SEQ ID NO: 2, one of skill in the art would require further research to actually determine if the biological function of the polypeptide of SEQ ID NO: 2 is indeed that of a thrombospondin. Furthermore, even if the polypeptide of SEQ ID NO: 2 is a thrombospondin, it is unclear as to how one of skill in the art can reasonably conclude that the claimed polynucleotides have a specific and substantial utility, if the specification is completely silent in regard to the type of thrombospondin disclosed, its biological target, the biological processes where it is involved or which diseases/disorders are associated with its expression, or lack thereof. In

regard to other uses such as forensics, paternity determination, and human biology, as indicated above and reiterated herein, that the specification is completely silent in regard to essential information which would allow one of skill in the art to use the claimed polynucleotides as asserted by Appellants. Specifically, the specification is completely silent as to any association between the presence or absence of these polymorphisms with a specific subset of the population, any identifying characteristic associated with such polymorphisms, such as ethnic background, X or Y chromosomal linkage, frequency within a population, or disorders/diseases associated with their presence or absence.

In regard to Appellant's assertions that there is a contradiction between the Final Action (Paper No. 13, mailed on 12/3/2002) on page 3 and the Advisory Action (Paper No. 17 mailed on 6/3/2003) on page 4, lines 10-15, it is noted for the record, that page 3 of the Final Action does not contain a statement, as asserted by Appellants, indicating that the specification does not disclose a function. The only reference to thrombospondin activity is made on page 4, lines 5-9, and reads as follows : "Therefore, it appears that there is no evidence to clearly support Applicant's assertion in regard to function. Furthermore, Applicants have not disclosed which type of thrombospondin is encoded by the polynucleotide of SEQ ID NO: 1 since it is known in the art that these proteins belong to a family of at least 5 members in vertebrates, each with diverse function". Since , as indicated by Appellants, the Advisory Action indicates that even if they polypeptide of SEQ ID NO: 2 is indeed a thrombospondin, the claimed invention would lack utility because thrombospondins belong to a family of at least 5 members in vertebrates and the specification is silent in regard to the type of thrombospondin disclosed in the specification, it is unclear to the Examiner as to which contradiction is being referred to by Appellants.

On page 7 of the Brief, last paragraph, and continuing on page 8, Appellants submit that the Advisory Action cites publications that disclose several examples regarding the unpredictability of assigning function based on structure as small changes can lead to changes in function, however, Appellants submit that none of these examples are thrombospondins. Appellants also submit that the

teachings of Witkowski et al. (Biochemistry 38:11643-11650, 1999), Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995), Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001), and Broun et al. (Science 282:1315-1317, 1998) are mere examples of a small number of spurious publications (1) that call into doubt the usefulness of function based on shared structure and bioinformatic predictions and (2) that the PTO has repeatedly attempted to use as a basis to deny the utility of polynucleotides. Appellants point out that the lack of 100% unanimous agreement on the usefulness of shared structure and bioinformatic prediction does not indicate that the claimed polynucleotides lack specific and substantial utility. According to Appellants, the legal test for utility simply involves an assessment of whether one of skill in the art would find any of the utilities described in the specification to be believable and argue that the majority of those of skill in the art would believe bioinformatic prediction to be a powerful tool as evidenced by thousands of journal articles.

While the Examiner agrees that the examples taught by Broun et al., Van de Loo et al., Seffernick et al. and Witkowski et al., do not specifically refer to thrombospondins, the Examiner disagrees with Appellant's contentions that the instant references are mere examples of a small number of spurious publications (1) that call into doubt the usefulness of function based on shared structure and bioinformatic predictions and (2) that the PTO has repeatedly attempted to use as a basis to deny the utility of the claimed polynucleotides. It is noted that the instant references were not provided as examples of thrombospondins but rather as specific examples which provide support to the general consensus in the art, as disclosed by Bork (cited in Paper No. 10 mailed on 5/14/2002), that accurate function annotation based on structural homology is still unpredictable. Therefore, contrary to Appellant's assertion that these references are spurious publications which cast doubt on the usefulness of function based on shared structure and bioinformatic predictions, the references by Broun et al., Van de Loo et al., Seffernick et al. and Witkowski et al., teach specific examples of enzymatic activity which was mistakenly predicted by

structural homology, and are evidence of the general state of the art in regard to function annotation based on structural homology (i.e. sequence homology), as disclosed by Bork.

The Examiner is not contending that one of skill in the art would not recognize the usefulness of bioinformatic predictions or that the claimed polynucleotides lack specific and substantial utility because there is no 100% unanimous agreement on the usefulness of shared structure and bioinformatic prediction. Also, the Examiner is not contending that there are not instances where function has been accurately predicted based on structural homology nor stating that structural homology is never sufficient for one of skill in the art to believe an assertion of function based thereon. However, as taught by the art presented by the Examiner, at the present time, with the tools currently available, there is no general consensus as to which genes are going to be easier to annotate using structural homology or which are the conditions required for functional annotation using structural homology to be highly predictable for any gene, except for the level of structural homology. As shown by the examples provided by the Examiner, even structural homologies ranging from about 60% to 98% have been found to be not sufficient to accurately predict function in all instances. While the Examiner has presented examples where even 1 amino acid substitution can result in a different function, one of skill in the art is more likely to conclude that a particular polynucleotide encodes a protein of a certain function if the functional homologs have a high degree of structural (i.e. sequence) similarity or if certain motifs specific to that function are present. In the instant case, however, the closest experimentally determined functional homolog of the polypeptide of SEQ ID NO: 2 is at best 5% sequence homologous and the specification is silent in regard to which are the structural elements in the polypeptide of SEQ ID NO: 2 that are associated to thrombospondin activity. This very low level of homology (5%), in addition to the fact that the procollagen I N-proteinase disclosed by Colige et al.(PIR accession number T18517, October 15, 1999) presents 4.9% sequence identity to the polypeptide of the instant application, is such that a skilled artisan would not find the

assertion in regard to the function of the polypeptide of SEQ ID NO: 2 probable, absent some further corroborating evidence.

The requirements under 35 USC § 101 and the current utility guidelines are that the claimed invention should have a credible, specific and substantial, or a well established utility. While credibility is not been questioned herein, it is noted that for the reasons previously discussed above, specifically the lack of information as to the thrombospondin type, targets, biological processes, disorders/diseases associated with the expression of the claimed polynucleotides, or lack thereof, as well as the lack of information in regard to how to use the claimed polynucleotides in forensics, human population biology or paternity determination, the claimed invention has not been found to have a specific and substantial utility. In view of the extremely low sequence homology between the polypeptide of SEQ ID NO: 2 and the closest experimentally-determined thrombospondin homolog, the fact that a polypeptide having procollagen I N-proteinase function has almost the same low structural homology to the polypeptide of SEQ ID NO: 2 as that of the closest thrombospondin (4.9%), combined with the lack of supporting experimental evidence in regard to the asserted biological function, and the unpredictability of the art in regard to accurately determining function based on structural homology, further research would be required to determine if indeed the claimed polynucleotides encode a thrombospondin and if so, which are its targets and biological function. Therefore, the asserted utility is not considered a substantial utility. Thus, contrary to Appellant's assertion, the claims do not meet the utility requirements under 3 5USC § 101.

On page 8 of the Brief, first paragraph, Appellants argue that the Federal Circuit in *Juicy Whip Inc. v. Orange Bang, Inc.* has stated that the threshold of utility is not high and that an invention is useful under section 101 if it is capable of providing some identifiable benefit. Appellants further cite *Brooktree Corp. v. Advanced Micro Devices, Inc.* to indicate that the Federal Circuit has stated that a claimed device must be totally incapable of achieving a useful result to lack utility under 35 USC § 101. Appellants cite

Cross v. Iizuka in support of the argument that any utility for a claimed invention is sufficient to satisfy the requirements of 35 USC § 101 and indicate that the Federal Circuit has confirmed that anything under the sun made by man is patentable in *State Street Bank & Trust Co. v. Signature Financial Group, Inc.*

The Examiner acknowledges the numerous cases cited by Appellants wherein issues in regard to 35 USC § 101 were examined. It is noted however that only *Cross v. Iizuka* is considered relevant to the instant discussion since the inventions in that case are chemical compounds. In *Juicy Whip Inc. v. Orange Bang, Inc.*, the issue of utility was discussed in regard to a juice dispenser, *in Brooktree Corp. v. Advanced Micro Devices, Inc.*, the issue of utility was discussed in regard to a digital to analog conversion circuitry, and in *State Street Bank & Trust Co. v. Signature Financial Group, Inc.*, the issue of utility was discussed in regard to a business method.

In *Cross v Iizuka*, the issues which the Federal Circuit had to examined were whether the Board erred in finding that the utility disclosed in the Japanese priority application by Iizuka is sufficient to meet the practical utility requirement of 35 U.S.C. §101 and whether the Board erred in finding that the Japanese priority application contained sufficient disclosure to satisfy the enablement, i.e., how-to-use, requirement of 35 U.S.C. § 112. The PTO, the Board of Patent Appeals and Interferences and the Federal Circuit found that the claimed imidazole derivative compounds had practical *in vitro* utility since in addition to the disclosure of the structure of the claimed imidazole derivative compounds, there was experimental evidence of the strong inhibition of thromboxane synthetase by these imidazole derivatives in human and bovine microsomes. Thromboxane synthetase is an enzyme which leads to the formation of thromboxane A 2, which at the time the applications of Cross and Iizuka were filed, was postulated to be a causal factor in platelet aggregation, which in turn, is known to be associated with platelet thrombosis, pulmonary vasoconstriction or vasospasm, inflammation, hypertension, and collagen-induced thrombosis. In contrast, the instant application discloses the structure of the claimed polynucleotides and no biological characterization of the polypeptide encoded by the claimed polynucleotides other than

to state that based on sequence homology it appears to be a thrombospondin. For the reasons indicated above, even if one assumes that the polypeptide encoded by the claimed polynucleotides is a thrombospondin, the specification fails to provide sufficient information for one of skill in the art to know how to use the claimed invention. The specification is silent in regard to (1) the specificity of the alleged thrombospondin, i.e. target, (2) the biological processes or pathways in which the alleged thrombospondin is involved, or (3) the disorders or conditions associated with the alleged thrombospondin. Information in regard to biological function and/or condition/disorders associated with the alleged thrombospondin is essential for the asserted utility in DNA chips or gene mapping, to be specific and substantial for the reasons already discussed above. While one of skill in the art can reasonably conclude that the chemical compounds of Iizuka had a credible, specific and substantial utility, i.e. the imidazole derivative compounds inhibit an specific enzyme, thromboxane synthetase, in human and bovine microsomes, a skilled artisan cannot reasonably conclude that the claimed polynucleotides have a specific and substantial utility or a well-established utility in view of the evidence presented.

On page 8 of the Brief, last paragraph and continuing on pages 9 and 10, Appellants submit that the legal test for utility simply involves an assessment of whether those of skill in the art would find any of the utilities described to be credible or believable. Appellants cite *In re Brana* in support of the argument that while further research and development may be needed, this does not preclude a finding that the invention has utility and state that the Federal Circuit admonished the PTO for confusing the requirements under the law for obtaining a patent and those required for government approval to market a drug for human consumption. Appellants further cite *In re Angstadt and Griffin, Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, and *In re Wands* in support of the argument that a considerable amount of experimentation is permissible if such experimentation is routinely practiced in the art and that a patent need not to disclose what is well known in the art.

As indicated above, while credibility is not been questioned herein, for the reasons previously discussed, specifically (1) the lack of information as to the type of thrombospondin disclosed in the specification, its targets, biological processes, disorders/diseases associated with the expression of the claimed polynucleotides, or lack thereof, (2) the lack of information in regard to how to use the claimed polynucleotides in forensics, human population biology or paternity determination, (3) the extremely low sequence homology between the polypeptide of SEQ ID NO: 2 and the closest experimentally-determined thrombospondin homolog, (4) the lack of supporting experimental evidence in regard to the asserted biological function, and (5) the unpredictability of the art in regard to accurately determining function based on structural homology, one of skill in the art cannot reasonably conclude that the asserted utility is specific nor can one of skill in the art reasonably conclude that the asserted utility is substantial since further research would be required to determine if indeed the claimed polynucleotides encode a thrombospondin, and if so, which are its targets and biological function.

The Examiner acknowledges the findings in *In re Brana*, *In re Angstadt and Griffin*, *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, and *In re Wands*. However, the Examiner disagrees with Appellant's contention that the claimed invention has utility in view of these findings. While it is agreed that FDA approval is not a requirement for finding a compound patentably useful and that routine experimentation does not render an invention unpatentable, it is noted that in the instant case, the utility rejection was not applied to the claimed invention because it failed to comply with government requirements to market the invention for human consumption or because some routine experimentation is required to practice the claimed invention. Instead, the utility rejection was applied due to the lack of information as to its biological function/use as discussed in claim rejections under 35 USC § 101 above. Furthermore, in regard to *In re Angstadt and Griffin*, *and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, even if one considers Appellant's assertion that the claimed polynucleotides can be used as polymorphic markers for forensics or for paternity determination, in view of the complete lack of information as to which specific

populations can be distinguished by the polymorphic markers disclosed, the frequency of these polymorphisms in a particular population, the biological role of these polymorphisms, whether they are X or Y chromosome linked, or which identifying characteristics are associated with the absence or presence of these polymorphisms such that one can distinguish one individual from another, one of skill in the art cannot reasonably conclude that the additional research required to practice the claimed invention is merely routine experimentation. In regard to *In re Brana*, it is noted that "the expectation of further research and development" as recited in the decision by the Federal Circuit refers to additional research to determine if the invention is safe and effective in humans, which are FDA requirements for market approval, and does not refer to further research and development to determine how to use the invention, which is the case herein. In regard to *In re Wands*, while it is agreed that one need not to disclose what is well known in the art, it is noted that neither the specification nor the state of the art describe or provide any information as to (1) the actual biological function of the polypeptide encoded by the claimed polynucleotides other than to indicate that the polypeptide of the instant invention shares structural homology to mammalian thrombospondins, (2) the biological role of the polymorphisms disclosed, (3) which populations can be distinguished by the polymorphic markers disclosed and their frequencies in such populations, (4) whether these are X or Y chromosome linked polymorphisms, or (5) which identifying characteristics are associated with the presence or absence of these polymorphic markers. Since information which would enable one of skill in the art to practice the claimed invention is not known in the art, it is the specification which must provide the necessary information to enable the skilled artisan to practice the claimed invention.

On page 10 of the Brief, first paragraph, and continuing on page 11, Appellants submit that the Final and Advisory Actions seem to be requiring Appellants to identify the biological role the claimed polynucleotides or its corresponding polypeptide before they can be used in gene chip applications. Appellants point out that knowledge of the exact function or role of the present polynucleotides is not

required to track expression patterns using a DNA chip. According to Appellants, given the widespread utility of gene chip methods using public domain gene sequence information, there can be no doubt of the great utility of the claimed polynucleotides in DNA chip applications. Appellants also submit that the claimed polynucleotides provide specific markers of the gene and provide unique identifiers of the corresponding gene in the human chromosome. Furthermore, Appellants submit that these specific markers are targets for drug discovery and that these polynucleotides are ideal candidates for assessing gene expression using DNA chips. These chips, according to Appellants have utility as evidenced by hundreds of issued patents exemplified in Exhibits A-F.

According to Appellants even negative information has great "real world" practical utility and knowing that a given gene is not expressed in medically relevant tissue provides an informative finding of great value to industry by allowing for more efficient deployment of resources. While it is agreed that (1) public domain gene sequence information is used in gene chip applications, (2) knowing that a given gene is not expressed in certain tissues provides useful information, (3) tracking gene expression does not require knowing its biological function, and (4) many patents related to gene chip technology, such as those in Exhibits A-F have been issued, the Examiner disagrees with Appellant's contention that the claimed polynucleotides have utility in gene chip applications since they are specific markers which are targets for discovering drugs associated with human disease. The Examiner is not disputing the patentable utility of DNA chips as a collection of polynucleotides linked to a solid support but rather the patentable utility of specific polynucleotides encoding an alleged thrombospondin. The Examiner acknowledges the hundreds of issued patents in regard to DNA chips however it is noted that the instant claims are not drawn to methods of use of DNA chips or to DNA chips (microarrays) but rather to specific polynucleotides. Furthermore, the asserted use of the claimed polynucleotides in DNA chips is not specific since as Appellants have stated, many other polynucleotides including those in the public domain can and are used in DNA chips. As indicated by the Examiner in previous Office Actions, for the claimed

polynucleotides to be specifically useful in DNA chip applications, one would require some knowledge or guidance as to the biological role of the polypeptide encoded by such polynucleotides to effectively use the information gathered in tracking the expression patterns of such polynucleotides. The reduction or increase in expression of a polynucleotide is meaningless unless one can link changes in expression with some biological function. For example, if one were to use the claimed polynucleotides in assays which would lead to the discovery of drugs for a specific condition, such as an assay which uses a DNA chip to evaluate expression patterns upon exposure to a test compound, one needs to know which diseases and/or biological functions are associated with the expression of such polynucleotides. Otherwise, one of skill in the art would have to carry out further experimentation to determine which are the conditions (i.e. diseases) and/or biological functions associated with the claimed polynucleotides. Appellant's contention that the claimed polynucleotides have utility in gene chip applications since they are specific markers which are targets for discovering drugs associated with human disease is not persuasive since the specification is silent in regard to (1) the conditions and/or biological functions which are associated with the expression of the claimed polynucleotides, (2) whether increase or decrease in expression correlates with disease, (3) which levels of increase or decrease in expression of the claimed polynucleotides are indicative of the presence or absence of a disease, and (4) how is the claimed invention a marker of the human genome. This is analogous to the examples provided by MPEP § 2107.01 in regard to what constitutes carrying out further research to identify or reasonably confirm a "real world" context of use since basic research is required to determine the properties or the mechanisms in which the claimed product is involved. Therefore, it is unclear how one of skill in the art can reasonably conclude that the asserted use of the claimed polynucleotides in DNA chips is a specific and substantial utility.

On page 11 of the Brief, first paragraph, Appellants submit that only a small percentage of the genome encodes exons. Thus, according to Appellants, not all human genomic DNAs are useful in gene chip applications. Therefore, it is Appellant's opinion that this is evidence which shows that such uses are

not generic, as asserted by the Examiner. Appellants further cite *In re Langer* and *In re Marzocchi* to support the argument that a statement of utility in a specification must be accepted absent reasons why one of skill in the art would have reason to doubt truth of such statement.

While the Examiner agrees that only a small portion of the genome encodes proteins, as admitted by Appellants, other polynucleotides comprising exons can be used in gene chips. Furthermore, as known in the art, gene chips can comprise polynucleotides which do not comprise exons. As indicated above and reiterated herein, for the claimed polynucleotides to be specifically useful in DNA chip applications, one would require some knowledge or guidance as to the biological role of the polypeptide encoded by such polynucleotides to effectively use the information gathered in tracking expression patterns. In regard to the findings in *In re Lager* and *In re Marzocchi*, it is reiterated that credibility has not been assessed. The Examiner deemed the claimed invention as lacking utility in view of the fact that the claimed polynucleotides do not have a specific and substantial or well-established utility, for the reasons discussed above.

On page 11 of the Brief, second paragraph, Appellants argue that evidence of "real world" substantial utility is further provided by the fact that there is an entire industry based on the use of genes or fragments thereof in a gene chip. Appellants refer to many companies known to use gene chip technology and assert that in view of the fact that these companies are worth millions of dollars, there is a "real world" substantial industrial utility associated with such genes and fragments thereof. Appellants further indicate that persons of skill in the art as well as venture capitalists would readily recognize the utility of genomic data, especially human. Appellants refer to Exhibits G (Venter et al.) and H (Jasny et al.) in support of the argument that billions of dollars have been spent in the human genome project and that the results have been a stunning success since the utility of the genomic data has been widely recognized as a great gift to humanity. Appellants conclude that the usefulness of human genomic data such as what is disclosed by the specification is substantial, credible and well-established.

While the Examiner acknowledges that (1) there is an entire industry based on the use of gene chip technology, (2) many companies using this technology are worth millions of dollars, (3) one of skill in the art as well as venture capitalist and investors can recognize the utility of genomic data,(4) the teachings of Venter et al. and Jasny et al, (5) billions of dollars have been spent in the generation of human genomic data, (6) the utility of human genomic data, Appellant's arguments have not been found persuasive for the following reasons. First, it is noted that commercial success is not one of the requirements for utility under 35 USC § 101. The Examiner is not disputing that one of skill in the art can see the potential usefulness of information coming out of the human genome project, however it is also known in the art that this information is valuable to the extent that it provides a starting point for scientists to further investigate the biological significance of the genetic information collected and possibly discover how to treat many conditions and diseases. In fact, while the potential usefulness of human genomic data was enormous, the lack of an immediate use for human genomic data was the primary reason why it was the federal government and not a private entity who first provided funding for the Human Genome Project. While it is agreed that the disclosure of an additional human polynucleotide provides more information in regard to the human genome, as indicated previously, in the absence of any additional information in regard to its biological function, the isolation of the human polynucleotides of the instant application is only useful as a starting point for researchers to further investigate its biological significance, therefore the utility of the instant polynucleotides, as clearly stated in MPEP § 2107.01 is not a "real world" substantial utility.

On page 12 of the Brief, first paragraph, Appellants argue that while only one utility is needed to meet the requirements of 35 USC § 101, the claimed polynucleotides have specific utility in determining the genomic structure of the corresponding human chromosome and for mapping the protein encoding regions. Appellants submit that the claimed polynucleotides provide exquisite specificity not shared by virtually any other nucleic acid. Appellants state that early gene mapping techniques do not provide

sufficient resolution to detect specific genes involved in disease and that a significant benefit is afforded by the claimed polynucleotides as markers of a specific locus of the human genome.

The Examiner acknowledges that (1) earlier mapping techniques may not provide high resolution, and (2) the claimed polynucleotides can be used to detect a human chromosome and a particular locus within that human chromosome. However, the Examiner disagrees with Appellant's contention that the claimed polynucleotides have utility for the following reasons. First, the specification is completely silent as to which human chromosome contains the claimed polynucleotide. Even if the human chromosome which contains the polynucleotide of SEQ ID NO: 1 is known, while the polynucleotide of SEQ ID NO:1 can be used as a marker to detect the corresponding human chromosome since such chromosome contains the locus of the gene encoding the polypeptide of SEQ ID NO:2 (encoded by the polynucleotide of SEQ ID NO:1), that chromosome also contains other genes. As such, any polynucleotide which is complementary to any of those genes can be used as a marker of such chromosome. Similarly, any of those genes contained in that chromosome can be used for gene mapping and would also have the ability to localize a particular region of such chromosome. Therefore, unless there is some information as to the biological role and/or the conditions/disorders associated with that particular locus in that human chromosome, or some information is provided in regard to how the claimed polynucleotides are specific markers of the human genome, the asserted uses of the claimed polynucleotides cannot be considered specific and substantial.

On page 12 of the Brief, second paragraph and continuing on page 13, Appellants indicate that only a minor percentage of the genome actually encodes exons. As such, the claimed polynucleotides provide biologically validated empirical data that specifically defines that portion of the corresponding locus that actually contains an exon. Appellants also submit that the claimed polynucleotides define how the exons are spliced together to produce an active transcript. Therefore, according to Appellants, the claimed polynucleotides have practical scientific value in regard to the significance of expressed sequence

information for structural analysis, as evidenced by Venter et al. In addition, Appellants refer to the Advisory Action, and submit that while the Examiner recognizes that the claimed polynucleotides can be used to detect the specific locus which contains the corresponding gene, the Examiner does not recognize the value of this specific and substantial utility for identifying protein encoding regions. Appellants indicate that the specification on page 3, lines 10-18 describes that the claimed polynucleotides are expressed in human cell lines, human brain, fetal brain, pituitary, cerebellum, spinal cord, thymus, spleen, trachea, kidney, liver, thyroid, adrenal gland, salivary gland, heart, uterus, stomach, small intestine, placenta, mammary gland, adipose, skin, esophagus, cervix, pericardium, fetal lung, and gene trapped human cells. Therefore, Appellants conclude that the claimed polynucleotides are expressed mRNA transcripts.

The Examiner acknowledges that (1) only a minor percentage of the genome actually encodes exons, and (2) information regarding expressed polynucleotides is of great importance in structural analysis of genomic data. However, it is noted that it is the patentable utility of specific polynucleotides encoding an alleged thrombospondin and not the significance of additional information in regard to additional coding sequences which is being determined and discussed. Furthermore, while it is agreed that the specification discloses that the claimed polynucleotides were found in different cells, there is no information as to how the mRNA was obtained, whether these polynucleotides were identified in a cDNA library from these cells or how this cDNA library was constructed. As known in the art, cDNA libraries can contain cDNAs which may not be representative of the actual transcript of a gene (i.e. mRNA) since the PCR primers used in the construction of such libraries may contain parts of an intron and many other artifactual constructs can be produced during amplification of a library. As such, the cDNAs produced, while containing exons, may not be representative of an actual transcript as they may also contain parts of an intron or present artifactual junctions which are not naturally produced, therefore resulting in a wrong transcript of a gene. In the absence of additional experimental evidence corroborating that the

claimed polynucleotides are indeed actual transcripts of a gene, one cannot reasonably conclude that the claimed polynucleotides provide biologically validated data. However, even if it is assumed that the claimed polynucleotides are indeed the actual transcript of a gene, as indicated previously, in the absence of any additional information in regard to its biological function, the isolation of the human polynucleotides of the instant application is only useful as a starting point for researchers to further investigate its biological significance, therefore the utility of the instant polynucleotides, as clearly stated in MPEP § 2107.01 is not a "real world" substantial utility.

On page 13 of the Brief, last paragraph and continuing on page 14, Appellants refer to Exhibit I, which was presented as Exhibit C in response to the Final Action. Appellants submit that an alignment of SEQ ID NO: 1 to a specific human genomic sequence shows portions of the genome that encode the present invention and that the polynucleotide of SEQ ID NO: 1 comprises 7 exons spread non-contiguously along a region of human chromosome 20, at approximately 20q12, wherein said exons are disclosed in clones AL133463.16 and AL050320.19 (GenBank's entries AL133463 and AL050320, respectively). Therefore, it is Appellant's contention that one could not simply be able to identify these 7 exons or to map the protein coding regions without knowing what those specific sequences are. Furthermore, Appellants indicate that in the Advisory Action, the Examiner does not recognize the alignment presented as evidence which shows that the polynucleotide of SEQ ID NO: 1 is indeed an actual transcript of a gene. Appellants conclude that the alignment presented in Exhibit I and the fact that the claimed polynucleotides were detected by Northern analysis in some tissues but not others, indicates that these polynucleotides represent biologically validated transcripts.

First, as indicated above, it is important to note that the specification does not provide any information as to the actual genomic locus (i.e. chromosomal position of the gene) which corresponds to the claimed polynucleotides. Exhibit I is an alignment of the polynucleotide of SEQ ID NO:1 and fragments of chromosome 20 which were disclosed by different parties after the instant application was

filed. While it is agreed that (1) the alignment of Exhibit I appears to indicate that chromosome 20 contains the polynucleotide of SEQ ID NO: 1 at position 20q12, (2) the claimed polynucleotides can be used to map the corresponding human chromosome, which in this case appears to be chromosome 20, and (3) one would not be able to map the region of such chromosome containing the claimed polynucleotides without knowing the sequence disclosed in the specification, the Examiner disagrees with Appellant's contention that there is a specific and substantial utility for the claimed polynucleotides for chromosome and gene mapping, identification of protein encoding regions of the genome or intron/exon splice regions. Any human polynucleotide which encodes a protein can be used to detect the particular locus of the corresponding gene, therefore any human polynucleotide which encodes a protein can be used to detect exons, intron/exon junctions, as well as to determine the specific chromosome which contains that locus. In addition, while one could argue that the claimed polynucleotides can be used as markers to isolate the particular chromosome which contains the locus of the gene encoding the polypeptide of SEQ ID NO: 2 (encoded by the polynucleotide of SEQ ID NO:1), since that chromosome will contain many other genes, any polynucleotide which is complementary to any of those other genes will also serve as a marker for that particular chromosome. Similarly, any polynucleotide encoding a protein can be used to identify a protein coding sequence. Therefore, one cannot conclude that the asserted utilities are specific to the claimed polynucleotides. This situation is analogous to the examples provided in MPEP § 2107.01 in regard to what constitute a non-specific utility since, as stated MPEP § 2107.01 "a specific utility is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to a broad class of inventions". Therefore, unless there is some information as to the biological role and/or the conditions/disorders associated with that particular locus in chromosome 20, or some information is provided in regard to how the claimed polynucleotides are specific markers of the human genome, the asserted uses of the claimed polynucleotides cannot be considered specific. In addition, in the absence of any additional information in regard to its biological function, the isolation of the human polynucleotides

of the instant application is only useful as a starting point for further experimentation and research. As such, the asserted utilities for chromosomal/gene mapping, identification of protein-encoding regions, detection of intron/exon junctions cannot be considered specific and substantial utilities.

On page 14 of the Brief, last paragraph, and continuing on page 15, Appellants indicate that while they are aware of the new utility guidelines set forth by the USPTO, the current rules and regulations are the patent laws set forth in 35 USC and the rules set forth in 37 CFR but not the Manual of Patent Examination Procedure (MPEP) set forth by the USPTO. Furthermore, Appellants argue that it is the job of the judiciary and not the USPTO to interpret these laws and rules. Appellants argue that there are no recent changes in either 35 USC § 101 or in the interpretation of 35 USC § 101 by the Supreme Court or the Federal Circuit which support the new utility guidelines set forth by the USPTO and submit examples of US patents in Exhibit L, M, N and O, which, according to Appellants, do not comply with the new utility guidelines. While Appellants admit that each application is examined on its own merits, Appellants conclude that holding them to a different standard of utility is a clear violation of due process due to the similarity in subject matter between the claimed invention and the inventions in US patents of Exhibit J, K, L, and M.

Appellants are reminded that the Examiner must examine a patent application according to the guidelines set forth by the USPTO as well as the MPEP, since the Examiner has no authority to disregard such guidelines or to apply her own interpretation of patent law in the examination of the application. Furthermore, as set forth in the guidelines and the MPEP, the guidelines were promulgated by the PTO in accordance with all applicable case law and thus are believed to be consistent therewith. While the Examiner acknowledges the US patents of Exhibits J, K, L, and M, as indicated in previous Office Action Paper No. 13 (Final Rejection), mailed on 12/3/2002 and Paper No. 17 (Advisory Action), mailed on 6/3/2003, each application is examined on its own merits according to the current guidelines of examination as set forth by the USPTO and a discussion on the utility of any polynucleotide claimed in

such patents would require a detailed review of the record of each individual case, which would be improper herein. Finally, Appellants are further reminded that the Examiner has no authority to comment in regard to the legality of the new utility guidelines or the MPEP as set forth by the USPTO.

B. Are Claims 2-3 and 6-7 unusable by a skilled artisan due to a lack of patentable utility?

At the beginning of page 16 of the Brief, Appellants indicate that arguments detailed in section VIII(A) of the Brief are incorporated by reference due to the fact that it has been determined by the courts that the utility requirement of Section 101 and the how to use requirement of Section 112, first paragraph have the same basis. Appellants argue that since claims 2-3 and 6-7 have been shown to have a "specific, substantial and credible utility" as indicated in section VIII(A), the present rejections under 35 USC 112, first paragraph cannot stand.

As indicated by Appellants, a rejection under § 112, first paragraph, may be affirmed on the same basis as a lack of utility rejection under § 101. *See, e.g., In re Swartz*, 56 USPQ2d 1703 (Fed. Cir. 2000); *In re Kirk*, 153 USPQ 48 (CCPA 1967).

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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